PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/US2004/020491	International filing date *(day/month/year)* 25.06.2004
Priority date *(day/month/year)* 26.06.2003	
International Patent Classification (IPC) or both national classification and IPC A61K39/118, A61K39/40	
Applicant CHIRON CORPORATION	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Mata Vicente, T.

Telephone No. +31 70 340-3377

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/020491

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

   see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/020491

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18-21

because:

☒ the said international application, or the said claims Nos. 18-21 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. (1, 3-22) - partially

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1, 3-22
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1, 3-22
Industrial applicability (IA)	Yes:	Claims	1, 3-17 and 22
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item I
Basis of the report

In the letter dated 9.11.2004 the statement indicating that no new subject matter has been added is missing.

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 18-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV
Lack of unity of invention

The IPEA agrees with the lack of unity objection raised by the ISA in the SR for the following reasons:

The following separate groups of inventions have been identified in the present application "a priori":

Problem 1: Further provision of vaccines against C. trachomatis. **Solutions (Claims 1-22):** Immunogenic composition comprising combinations of between two and thirteen of the *Chlamydia trachomatis* antigens PepA, LcrE, ArtJ, DnaK, CT398, OmpH-like, L7/L12, OmcA, AtoS, CT547, Enolase, HtrA and MurG. Vaccines comprising said immunogenic composition. Use thereof in methods of treatment/diagnosis/prevention of C. trachomatis infection.

Problem 2: Further provision of vaccines against sexually-transmissible diseases. **Solution (Claims 23-25):** Immunogenic composition comprising an oligonucleotide containing a CpG motif, a mineral salt and an antigen associated with a sexually transmitted disease.

Moreover, vaccines against C. trachomatis are known in the prior art (see WO03049762,

Brunham and Eko et al.). And even further, the immunogenicity of the C. trachomatis antigens PepA, LcrE, ArtJ, DnaK, CT398, OmpH-like, L7/L12, OmcA, AtoS, CT547, Enolase, HtrA and MurG has also been described (WO03049762, Sanchez-Campillo et al.) and, as a consequence, the obvious use thereof in vaccination (WO03049762).

In the light of the prior art, the solutions to the first problem (already defined above) can be grouped as follows:

-Immunogenic composition comprising the combination of Chlamydia trachomatis antigens PepA+LcrE. Vaccines comprising said immunogenic composition. Use thereof in methods of treatment/diagnosis/prevention of C. trachomatis infection.

-Idem as subject 1, but restricted to each one of the combinations mentioned in Claim 1 except PepA+LcrE and PepA+LcrE+ArtJ+DnaK+CT398.

-Idem as subject 1 but restricted to the specific combination PepA+LcrE+ArtJ+DnaK+ CT398 according to Claim 2.

-Idem as subject 1 but restricted to the specific combination OmpH-like+L7/L12.

-Idem as subject 1 but restricted to the specific combination OmcA+AtoS.

-Idem as subject 1 but restricted to each one of the combinations mentioned in Claim 8 which are not covered by inventions 1-28.

Due to essential difference in the nature of the two problems and their corresponding solutions and due to the fact that no other technical feature can be distinguished which, in the light of the prior art, could be regarded as special technical feature common to these solutions.

Consequently, in the light of the above arguments the IPEA agrees with the objection put forward by the ISA. The present application is considered to relate to 8179 separate inventions which lack unity in the sense of Rule 13.1 PCT.

An opinion with regard to novelty, inventive step or industrial applicability will be given only with respect to the invention first mentioned in the claims, that is, to the following subject-matter: **Claims (1 and 3-22) - partially**: Immunogenic composition comprising the combinations of *Chlamydia trachomatis* antigens PepA+LcrE. Vaccines comprising said immunogenic composition. Use thereof in methods of treatment/diagnosis/prevention of C. trachomatis infection.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 03/049762 A (CHIRON SPA; GRANDI, GUIDO; RATTI, GIULIO; CHIRON SRL) 19 June 2003 (2003-06-19)

D2: BRUNHAM R C: "PROSPECTS FOR A CHLAMYDIAL VACCINE" PROGRAM AND ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, XX, XX, vol. 42, 27 September 2002 (2002-09-27), page 470, XP008042337

D3: EKO F O ET AL: "Recombinant Vibrio cholerae ghosts as a delivery vehicle for vaccinating against Chlamydia trachomatis" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 21, no. 15, 2 April 2003 (2003-04-02), pages 1694-1703, XP004413559 ISSN: 0264-410X

D4: SANCHEZ-CAMPILLO M ET AL: "IDENTIFICATION OF IMMUNOREACTIVE PROTEINS OF CHLAMYDIA TRACHOMATIS BY WESTERN BLOT ANALYSIS OF A TWO-DIMENSIONAL ELECTROPHORESIS MAP WITH PATIENT SERA" ELECTROPHORESIS, WEINHEIM, DE, vol. 20, no. 11, August 1999 (1999-08), pages 2269-2279, XP000900035 ISSN: 0173-0835

D5: MONTIGIANI S ET AL: "GENOMIC APPROACH FOR ANALYSIS OF SURFACE PROTEINS IN CHLAMYDIA PNEUMONIAE" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 70, no. 1, January 2002 (2002-01), pages 368-379, XP009032240 ISSN: 0019-9567

The document **D1** is regarded as being the closest prior art and discloses the identification of *C. trachomatis* antigens which can be used -alone or in combination- for vaccination or for diagnosis.

In view of the prior art cited, Claims 1 and 3-22 appear to be novel because they involve a specific immunogenic composition against *C. trachomatis* which is not diclosed in the prior art (i.e. PepA+LcrE) and, therefore, meet the requirements of Art. 33(2) PCT.

The problem to be solved by the present application may be regarded as the further provision of vaccines against *C. trachomatis* infection.

The difference between the subject-matter of **D1** and that of the present application lies in the immunogenic compositions that they respectively disclose.

Nevertheless, aware of the teachings of D2 and D3, which disclose multi-subunit vaccines against *C. trachomatis*, the skilled person would -in the light of D1- regard it a normal design procedure to combine several antigens known to be immunogenic and use said combination in a vaccine against chlamydial infection. In the view of the present Application the specific combination of *C. trachomatis* antigens herein disclosed do not appear to have any unexpected effect with respect to the individual antigens.

Therefore, Claims 1 and 3-22 cannot be regarded as involving an inventive step in the sense of Art. 33(3) PCT.

For the assessment of the present Claims 18-20 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII
Certain observations on the international application

The following objections are raised on the formulation of the claims for the sake of completeness of the examination procedure according to Art. 6 PCT:

The expression "one or more" (Claims 4, 9, 12, 13 and 22) add ambiguity to the range covered by the claims.

Claims 1 and 8 refer to "combinations of two, three... *C. trachomatis* antigens" mentioned in the respective claims. Said wording renders the scope of the claims entirely unclear and is not supported by the description.

The expression "herein incorporated by reference" and similar ones contained in the description (like on page 1, line 5; page 50, line 22; page 51, line 6; page 54, last line; page 82, line 6) imply that the patent specification is not self-contained regarding the essential features of the invention, thus contravening Art.5 PCT.

The vague and imprecise statements in the description on page 59 ("The present invention will be defined only...spirit of the invention") and page 82 ("Various modifications and variations...intended to be covered by the present invention") imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity of the claims (Article 6 EPC) when used to interpret them.